



F a c t s A b o u t

Postmenopausal Hormone Therapy

Choosing whether or not to use postmenopausal hormone therapy can be one of the most important health decisions women face as they age. As with taking any treatment, the decision involves carefully weighing the risks and benefits involved.

But, until recently, the picture of those risks and benefits has been unclear. Studies gave conflicting results about the therapy's effects on breast cancer, heart disease, and other conditions.



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Heart, Lung, and Blood Institute

Box 1

Oral Estrogen and Estrogen/Progestin Products*

Estrogen pills:		Progestin pills:		Estrogen plus progestin pills:	
Premarin	conjugated equine estrogens	Amen	medroxyprogesterone acetate	Premphase	conjugated equine estrogens and medroxyprogesterone acetate
Cenestin	synthetic conjugated estrogens	Cycrin	medroxyprogesterone acetate	Prempro	conjugated equine estrogens and medroxyprogesterone acetate
Estratab	esterified estrogens	Provera	medroxyprogesterone acetate	Femhrt	ethinylestradiol and norethindrone acetate
Menest	esterified estrogens	Micronor	norethindrone	Activella	17-beta-estradiol and norethindrone acetate
Ortho-Est	estropipate (piperazine estrone sulfate)	Nor-QD	norethindrone	Ortho-Prefest	17-beta-estradiol and norgestimate
Ogen	estropipate (piperazine estrone sulfate)	Aygestin	norethindrone acetate		
Estrace	micronized 17-beta-estradiol	Ovrette	norgestrel		
		Norplant	levonorgestrel		
		Prometrium	progesterone USP (in peanut oil)		
		Megace	megestrol acetate (not for uterine protection)		

*As of Fall 2000

Box 2

Gels, Creams, Patches, and Other Hormone Products*

Estrogen products:

Cream	Estrace	micronized 17-beta-estradiol
	Ortho Dienestrol	dienestrol
	Premarin	conjugated equine estrogens
Vaginal Tablet	Vagifem	estradiol hemihydrate
Vaginal Ring	Estring	micronized 17-beta-estradiol
Skin Patch	Alora	micronized 17-beta-estradiol
	Climara	micronized 17-beta-estradiol
	Esclim	micronized 17-beta-estradiol
	Estraderm	micronized 17-beta-estradiol
	Vivelle	micronized 17-beta-estradiol
	Vivelle-Dot	micronized 17-beta-estradiol

Progestin products:

Vaginal Gel	Crinone	progesterone
Injection	Depo-Provera	medroxyprogesterone acetate (not for uterine protection)
IUD	Mirena	levonorgestrel
	Progestasert	progesterone

Estrogen plus progestin products:

Skin Patch	Combipatch	17-beta-estradiol and norethindrone acetate
	Ortho-Prefest	17-beta-estradiol and norgestimate
Injection	Depo-Testadiol	testosterone and estradiol cypionate

*As of Fall 2000

In the summer of 2002, new findings emerged that have finally begun to fill in some of the picture's details. While much more remains to be learned, the findings offer women some guidance about the risks and benefits of using postmenopausal hormone therapy.

This fact sheet discusses those findings and gives you an overview of such topics as menopause, hormone therapy, and alternative treatments to the symptoms of menopause and various health risks that come in its wake. It also provides a list of sources you can contact for more information.

If you're on hormone therapy—whether short- or long-term use—you're bound to have a lot of concerns. This fact sheet will provide some information, but it's important to talk with your doctor or other health care

provider about your health profile. Being informed is one of the best ways you can protect your health.

Menopause and Hormone Therapy

As you age, significant internal changes take place that affect your production of the two female hormones, estrogen and progesterone. The hormones, which are important in regulating the menstrual cycle and having a successful pregnancy, are produced by the ovaries, two small, oval-shaped organs.

During the years just before menopause, known as perimenopause, your ovaries begin to shrink. Levels of estrogen and progesterone fluctuate as your ovaries try to keep up production of the hormones. You can have irregular menstrual cycles, along with unpredictable episodes of heavy bleeding during a period. Perimenopause usually lasts several years.

Eventually, your periods stop. Menopause marks the time of your last menstrual period. It is not considered the last until you have been period-free for 1 year without being ill, pregnant, breast-feeding, or using certain medicines, all of which also can cause menstrual cycles to cease. There should be no bleeding, even spotting, during that year. Natural menopause usually happens sometime between the ages of 45 and 54.

You also can undergo menopause as the result of surgery. A surgical procedure, called a hysterectomy, removes the uterus and sometimes the ovaries and fallopian tubes as well. You go through menopause if both of your ovaries are removed. Otherwise, the surgery does not affect menopause, which still occurs naturally.

Whether you go through menopause naturally or surgically, symptoms can result as your body tries to adjust to the drop in estrogen levels. These symptoms vary greatly—one woman may breeze through menopause with few symptoms, while another has difficulty. Symptoms may last for several months or years, or persist. The most common symptoms are hot flashes or flushes, sweats, and sleep disturbances. (A hot flash is a feeling of heat in your face and upper body, which may cause the skin to appear flushed or red as blood vessels

expand. Hot flashes that occur with severe sweating during sleep are called night sweats.) But the drop in estrogen also can contribute to other symptoms, such as changes in the vaginal and urinary tracts, which can cause painful intercourse, urinary infections, and the need to urinate more often.

To relieve the symptoms of menopause, doctors may prescribe postmenopausal hormone therapy. This can involve the use

Box 3

Hormone Therapy Schedules

- Cyclic or sequential—Estrogen for 25 or 30 days a month, with progestin added for 10-14 days
- Continuous-combined—Estrogen and progestin daily



Alternatives to Hormone Therapy to Help Prevent Postmenopausal Conditions and Relieve Menopausal Symptoms

You may want to consider alternatives to hormone therapy to ease menopausal symptoms. The list below includes some locally applied hormone products (which may not carry the same risks as those that deliver medication throughout the body), dietary supplements, and lifestyle measures. Talk with your doctor or other health care provider about the best treatment for you for each symptom.

Be aware that, unlike drugs, the U.S. Food and Drug Administration (FDA) does not have the authority to approve dietary supplements before they are sold. The dietary supplement manufacturer is responsible for insuring that the product is safe and that any representations or claims made about it are adequately substantiated and not false or misleading (see Box 5).

One positive move you can make to feel better is to adopt a healthy lifestyle—don't smoke, eat a variety of foods low in saturated fat and cholesterol and moderate in total fat, maintain a healthy weight, and be physically active.

For postmenopausal conditions:

Osteoporosis—

- See Box 20 for lifestyle behaviors to protect bone density
- Designer estrogen Raloxifene (Evista), which preserves bone density
- Bisphosphonates Actonel or Fosamax, which reverse bone loss and prevent fractures
- Calcitonin (a nasal spray), which may prevent fractures
- Note: Phytoestrogens (see “Hot flashes” below) have not been shown to reduce fractures

Heart disease—

- Lifestyle behaviors, including:
 - *Following a healthy eating plan
 - *Limiting consumption of alcoholic beverages
 - *Not smoking
 - *Maintaining a healthy weight
 - *Being physically active
- Preventing and controlling high blood pressure
- Preventing and controlling high blood cholesterol
- Managing diabetes
- Taking prescribed medication to control heart disease

For menopausal symptoms:

Hot flashes—

- **Lifestyle changes.** These include dressing and eating to avoid being too warm, sleeping in a cool room, and reducing stress. Avoid spicy foods and caffeine. Try deep

breathing and stress reduction techniques, including meditation and other relaxation methods.

- **Soy.** This contains phytoestrogens. (Phytoestrogens are estrogen-like substances derived from a plant source.) However, there is no solid evidence that soy—or other sources of phytoestrogens—really do relieve hot flashes. Further, the risks of taking soy, especially the more concentrated forms of soy, such as pills and powders, are not known. Phytoestrogens from soy can be consumed through foods or supplements. Soy food products include tofu, tempeh, soy milk, and soy nuts. These soy products are more likely to work on mild hot flashes.
- **Other sources of phytoestrogens.** These include such herbs as black cohosh, a member of the buttercup family, wild yam, dong quai, and valerian root.
- **Antidepressants,** such as Effexor, Paxil, and Prozac. These have been proved moderately effective in clinical trials.

Vaginal dryness—

- Vaginal lubricants and moisturizers (available over the counter).
- Products that release estrogen locally (such as vaginal creams, a vaginal suppository, called Vagifem, and a plastic ring, called an Estring)—these are used for more severe dryness. The ring contains a low dose of estrogen and may not protect against osteoporosis. It also must be changed every 3 months.

Mood swings—

- Lifestyle behaviors, including getting enough sleep and being physically active
- Relaxation exercises
- Antidepressant or anti-anxiety drugs

Insomnia—

- Over-the-counter sleep aids
- Milk products, such as a glass of milk or cup of yogurt—choose low- or fat-free varieties
- Do physical activity in the morning or early afternoon—exercising later in the day may increase wakefulness
- Hot shower or bath immediately before going to bed

Memory problems—

- Mental exercises
- Lifestyle behaviors, especially getting enough sleep and being physically active

of either estrogen alone or with another hormone called progesterone, or progestin in its synthetic form. The two hormones normally help to regulate a woman's menstrual cycle. Progestin is added to estrogen to prevent the overgrowth (or hyperplasia) of cells in the lining of the uterus. This overgrowth can lead to uterine cancer. If you haven't had a hysterectomy, you'll receive estrogen plus progestin therapy; if you have had a hysterectomy, you'll receive estrogen-only therapy. Hormones may be taken daily (continuous use) or on only certain days of the month (cyclic use).

They also can be taken in several ways, including orally, through a patch on the skin, as a cream or gel, or with an intrauterine device (IUD) or vaginal ring. How the therapy is taken can depend on its purpose. For instance, a vaginal estrogen ring or cream can ease vaginal dryness, urinary leakage, or vaginal or urinary infections, but does not relieve hot flashes.

Hormone therapy may cause side effects, such as bleeding, bloating, breast tenderness or enlargement, headaches, mood changes, and nausea. Further, side effects vary by how the hormone is taken. For instance, a patch may cause irritation at the site where it's applied.

Boxes 1 to 3 list products and schedules for various hormone therapies. There also are nonhormonal approaches to easing the symptoms of menopause. Box 4 offers a list of some of these alternatives.

Box 5

About Dietary Supplements

If you use dietary supplements to try to ease hot flashes and other menopausal symptoms, you should bear these points in mind: The U.S. Food and Drug Administration (FDA) does not have the authority to approve dietary supplements before they are marketed, and it's important to tell your health care provider that you are taking such remedies.



Dietary supplements are sold over the counter and may contain phytoestrogens: These are estrogen-like substances that come from some plants (such as soy) and plant materials (such as legumes, vegetables, cereals, and some herbs). For instance, these products may contain black cohosh, wild yams, dong quai, and valerian root.

Dietary supplement manufacturers are responsible for making sure that their products are safe. The FDA must show that a dietary supplement is harmful before it can limit the product's use or remove it from the market. Currently, there are no FDA regulations that specifically establish minimum standards for the manufacture of dietary supplements in order to insure their identity (tests to insure that the ingredient is actually what its label claims), purity, quality, strength, and composition. You may want to contact a product's manufacturer before buying it.

Furthermore, the possible effects of the products are not known. Some of the substances they contain are being studied. For example, soy contains plant estrogens, which are being studied to see if they have the same risks and benefits as estrogen.

Some of this research is being supported by the Office of Dietary Supplements, the National Center for Complementary and Alternative Medicine, the National Institute on Aging, and other units of the National Institutes of Health.

Until more is known about these substances, you should use them with caution. Also, as noted, tell your health care provider if you take a dietary supplement or if you increase your intake of dietary phytoestrogens. There may be dangerous side effects. An increase in the level of estrogens in your body could interfere with other prescription medications you are taking or even cause an overdose.

Postmenopausal Use

Menopause may cause other changes that produce no symptoms yet affect your health. For instance, a woman's risk of developing heart disease begins to rise around menopause. After menopause, women's rate of bone loss

increases. The increased rate can lead to osteoporosis, which may in turn increase the risk of bone fractures, usually after age 70.

Through the years, studies were finding evidence that estrogen might help with some of these postmenopausal health risks—

Box 6

What We Learn From Different Types of Studies

Medical researchers conduct many types of studies. The reason is that the studies yield different kinds of information. Together, the studies help scientists understand health and disease, and how to educate people so they can lead healthier lives.

Three main types are: observational studies, clinical trials, and community prevention studies. Each type is discussed briefly below:

■ **Observational studies** follow women's medical and lifestyle practices but do not intervene. Such studies can turn up possible relationships between various factors and health or illness. Those factors include population traits, ethnicity, genetic attributes, and behaviors. For instance, researchers can track women who do and do not take postmenopausal hormone therapy. The results may show that the hormone users have fewer heart attacks. But the results cannot conclude that hormone therapy reduces the risk of heart disease. Other factors may have played a part. For instance, compared with women who do not use hormone therapy, those who do are often healthier, have a higher level of education and better access to medical care, and are more willing to follow a prescribed therapy.

■ **Clinical trials** control and compare specific medical interventions, such as the use of postmenopausal hormone therapy. Women on an intervention are compared with those who do not receive the treatment. Researchers try to control all of the experimental conditions so that any difference between the two groups can be tied to the intervention.

The most rigorous of these investigations is the randomized, controlled, double-blinded clinical trial. Women are randomly assigned to the study groups and, in a drug trial for instance, neither the women nor the researchers typically know who is receiving an active drug and who a placebo. Further, on average women in the two groups will be similar in age, education, health at the time of entering the trial, and other factors that may affect the results. These trials are considered to be the "gold standard" among types of studies because they yield the most reliable information.

Clinical trials are often done to test whether a possible relationship uncovered in an observational study is in fact so. The trials help establish a causal link between a treatment and a specific medical outcome, such as fewer heart attacks.

■ **Community prevention studies** explore ways to encourage people to adopt healthier behaviors.



especially heart disease and osteoporosis. With more than 40 million American women over age 50, the promise seemed great.

Although erroneously thought of in the past as a "man's disease," heart disease is the leading killer of American women. Women typically develop it about 10 years later than men.

Similarly, menopause is a time of increased bone loss. Bone is living tissue. Old bone is continuously being broken down and new bone formed in its place. With menopause, bone loss is greater and, if not enough new bone is made, the result can be weakened bones and osteoporosis, which increases the risk of breaks. One of every two women over age 50 will have an osteoporosis-related fracture during her life.

Many scientists believed these increased health risks were linked to the postmenopausal drop in estrogen produced by the ovaries and that replacing estrogen would help protect against the diseases.

Early Findings

Early studies seemed to support hormone therapy's ability to protect women against the diseases that tend to occur after menopause. For instance, research showed that the treatment does prevent osteoporosis. However, other findings lacked evidence or were unclear. No large clinical trials had proved that hormone therapy prevents heart disease or fractures. Answers also were needed about other possible effects of long-term use of hormones, especially on such

Box 7

Risk Factors for Uterine Cancer

There are various types of uterine cancer. The most common is endometrial cancer, which begins in the lining (endometrium) of the uterus. It is often referred to as uterine cancer.

Key risk factors for uterine cancer are:

- Age—usually occurs after age 50
- Endometrial hyperplasia—an increase in cells in the lining of the uterus
- Hormone therapy—using estrogen without progesterone
- Obesity and related conditions
- Tamoxifen—taken to prevent breast cancer
- Race—white women are more likely than African American women to develop uterine cancer
- Colorectal cancer—those who have an inherited form are at a higher risk of developing uterine cancer
- Factors that increase exposure to estrogen—not having children, starting menstruation at an early age, entering menopause late

conditions as breast and colorectal cancers.

Further, prior research on postmenopausal hormone therapy’s effect on heart disease had involved mainly observational studies, which can indicate possible relationships between behaviors or treatments and disease, but cannot establish a cause-and-effect tie. (See Box 6 for more about types of studies.)

There also were some clinical trials, which are considered the

Box 8

Breast Cancer Risk Factors

About 80 percent of breast cancer cases occur after age 50. One of every eight American women who live to be 85 develops breast cancer. Some factors increase the risk for breast cancer. However, most women who develop breast cancer do not have any of the risk factors.

Key factors that increase the risk of developing breast cancer are:

- Personal history—if you’ve had it once, you’re more likely to develop it again
- Family history—if your mother, sister, or daughter had breast cancer, especially at an early age, you’re more likely to develop it
- Other breast changes (not including ordinary “lumpiness”)—such as atypical hyperplasia (an irregular pattern of cell growth)
- Genetic alterations—changes in certain genes, including BRCA1 and BRCA2 mutations

Other factors also may increase the risk of developing breast cancer. These include:

- Race—white women are more likely to develop it than African American or Asian women
- Estrogen exposure—risk is somewhat increased for those who began menstruation early (before age 12), had menopause late (after age 55), never had children, or took hormone therapy for long periods
- Late childbearing—having a first child after about age 30
- Radiation therapy—if given to the chest more than 10 years ago, especially in women younger than age 50
- Breast density—breasts with a high proportion of lobular and ductal tissue, which is dense and in which breast cancers usually appear
- Alcoholic beverage consumption



“gold standard” in establishing a cause-and-effect connection between a behavior or treatment and a disease. The most definitive clinical trials are those that test the effects of a treatment on the disease itself. But such clinical trials are time-consuming and costly. Consequently, early clinical trials of postmenopausal hormone use tested the therapy’s

effects on the risk factors or predictors of various diseases. One of the most important of these early clinical trials that tested effects on risk factors was the “Postmenopausal Estrogen/Progestin Interventions Trial,” or PEPI. Supported by the National Heart, Lung, and Blood Institute (NHLBI) and other units of the National Institutes of

Health (NIH), PEPI tested the effects of four hormone regimens (one estrogen-only and three different estrogen plus progestin regimens) on key risk factors for heart disease and bone mass. Begun in 1987, it followed 875 healthy, postmenopausal women, ages 45-64, for 3 years. About a third of the women had had a hysterectomy. Participants included various races but were predominantly white.

PEPI's results were generally positive:

- Each of the hormone regimens reduced “bad” LDL cholesterol and raised “good” HDL cholesterol, although estrogen-only raised good cholesterol the most. (LDL, or low density lipoprotein, carries cholesterol to tissues, including the arteries, while HDL, or high density lipoprotein, carries it away, aiding its removal from the body.)
- All hormone therapies decreased levels of fibrinogen. (High levels of fibrinogen allow blood clots to form more readily, thus increasing the risk of heart disease and stroke.)
- On the other hand, a large percentage of those who took estrogen alone had a high rate of overgrowth of the uterine lining and other abnormalities. This finding stressed the need for women with a uterus to use estrogen plus progestin therapy. The added progestin protects women against uterine cancer (see Box 7).

Box 9

WHI Findings On Estrogen Plus Progestin Therapy

Compared with a placebo, after about 5 years of use, estrogen plus progestin resulted in:

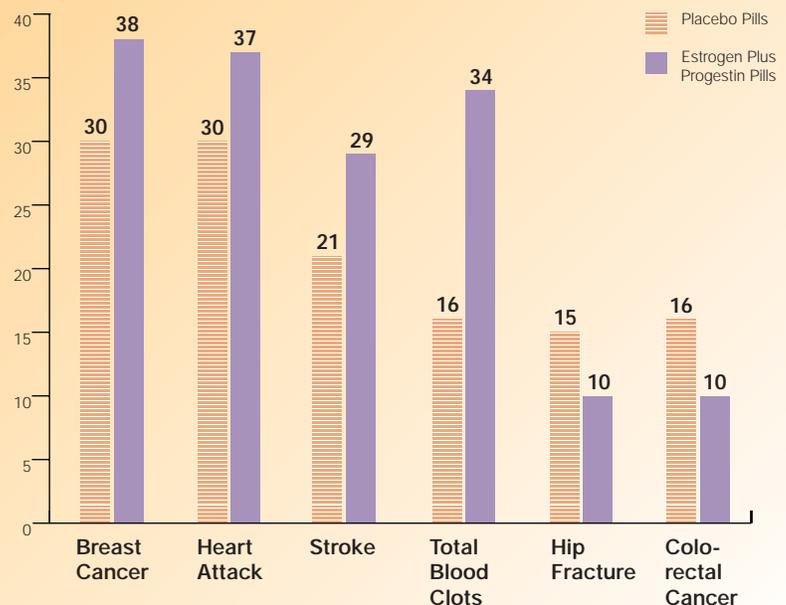
- | | |
|---------------------------|---|
| Increased risks | <ul style="list-style-type: none"> ■ 26% increase in breast cancer ■ 41% increase in strokes ■ 29% increase in heart attacks ■ Doubled rates of blood clots in legs and lungs |
| Increased benefits | <ul style="list-style-type: none"> ■ 37% less colorectal cancer ■ 34% fewer hip fractures |
| No difference | Number of deaths |



Box 10

Estrogen Plus Progestin Pills vs. Placebo Pills

The rate of the following medical conditions per 10,000 women per year



Box 11

What Do the Data Really Mean?

The data sound scary—and confusing. A 41 percent increase in strokes. A 34 percent decline in hip fractures. Which is more important? The bad news, or the good?

Either way, the percentages sound big. So it's good to take a moment and check out what they're really saying.

There are two main ways to express risk—"relative risk" and "absolute risk." The relative risk measures and compares the percent change in risk of some health-related event in a population that has been exposed to some agent and another that has not. The increase (or decrease) in absolute risk is an estimate of the number or proportion of women who will (or will not) develop a disease when exposed to a particular agent.

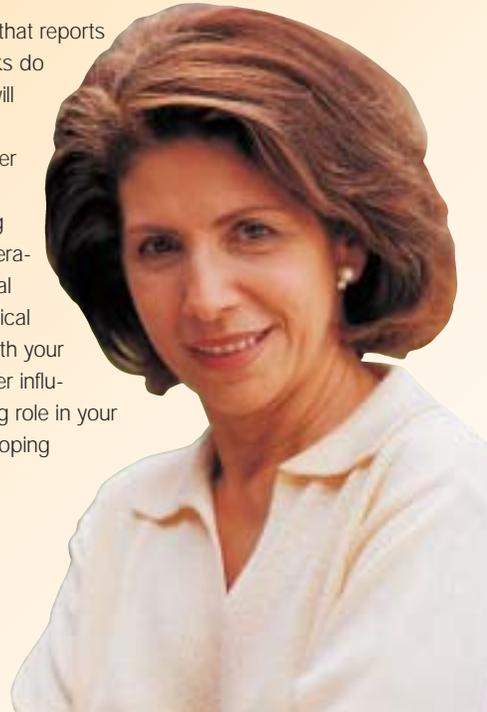
Relative risk allows scientists to compare data. In the WHI study, for example, scientists wanted to find out the relative risk of breast cancer in women who had and had not been exposed to the estrogen plus progestin hormone therapy. After about 5 years, the study had 166 cases of breast cancer among estrogen plus progestin users, compared with 124 in the placebo group. However, there were more women in the hormone group—8,506, compared with 8,102 in the placebo group. To be able to compare data from the groups, the cases were converted into rates per 10,000 women per year. Thus, the rate of breast cancer in the hormone group was 38 per 10,000 women, compared with 30 per 10,000 women in the placebo group. This also can be expressed as 38 divided by 30 or 1.26. Since that is 0.26 greater than an equal risk (or 1.00), the women on hormone therapy had a 26 percent greater chance of developing breast cancer than non-users.

What was the increase in absolute risk of developing breast cancer for women in the WHI study? On average, in any single year, 0.08 percent more women in the hormone group developed breast cancer than women in the placebo group. This means that, if a group of 10,000 women takes estrogen plus progestin for a year, there will be 8 more cases of breast cancer among the

hormone users than if they hadn't taken the therapy. Thus, women on the hormone therapy have only a slightly increased absolute risk of breast cancer over a year. (See Boxes 9 and 10 for a summary of the relative and absolute risks of breast cancer and other conditions for women in the estrogen plus progestin study.)

But, if you count up all the added cases of breast cancer, heart attacks, strokes, and blood clots in the lungs and subtract the fewer cases of colorectal cancer and hip fractures, you'd still get about 100 extra harmful events among the 10,000 hormone users after 5.2 years—the period the study ran. Multiply that by 10 years and millions of women and the number of cases of adverse effects grows.

Remember too that reports of increased risks do not mean you will develop breast cancer or another condition if you have been using the hormone therapy. Your personal and family medical history, along with your lifestyle and other influences, play a big role in your chance of developing a disease.



PEPI did not last long enough to tackle some crucial questions about hormone therapy, such as a possible rise in breast cancer risk (see Box 8).

The first clinical trial to investigate the effects of postmenopausal hormone therapy directly on diseases was the

“Heart and Estrogen-Progestin Replacement Study,” or HERS, which began enrolling participants in January 1983. HERS tested whether estrogen plus progestin would prevent a second heart attack or other coronary event. Altogether, it involved 2,763 postmenopausal women, average age 67, who already

had heart disease. The women received either estrogen plus progestin or a placebo for about 4 years. (A placebo is a substance that looks like the real drug but has no biologic effect.)

Findings, released in 1998, showed that those on the hormone therapy did not have fewer

Box 12

Risk Factors for Stroke

Main risk factors are:

- High blood pressure
- Diabetes
- Cigarette smoking

Other risk factors include:

- Family history—stroke appears to run in some families, whether due to genetics and/or shared lifestyle
- Heavy consumption of alcoholic beverages
- High blood cholesterol
- Menopause



Box 13

Risk Factors for Colorectal Cancer

About 30,000 women a year die of colorectal cancer—it is the third-leading cause of cancer deaths for women, after lung and breast cancers.

Factors that increase the risk of colorectal cancer include:

- Age—risk increases after age 50
- Diet—eating a diet high in fat and calories, and low in fiber
- Polyps—these are benign growths on the inner wall of the colon and rectum
- Personal medical history—having had cancer of the ovary, uterus, or breast; also having had colorectal cancer once increases the chance of developing it again
- Family medical history—having first-degree relatives (parents, siblings, or children) with colorectal cancer, especially at a young age; risk increases even more if many family members have had colorectal cancer
- Ulcerative colitis—a condition in which the lining of the colon becomes inflamed



fatal or nonfatal heart attacks. In fact, the women's risk for a heart attack increased during the first year of hormone use, declining thereafter. HERS also showed that the therapy caused an increase in blood clots in the legs and lungs.

More recently, the "HERS Follow-Up Study," which tracked the women for about 3 more years, found no decrease in heart disease from use of estrogen plus progestin therapy.

The Women's Health Initiative

In 1991, the NHLBI and other units of the NIH launched the "Women's Health Initiative" (WHI), one of the largest studies of its kind ever undertaken in the United States. It consists of a set of clinical trials, an observational study, and a community prevention study, which altogether involve more than 161,000 healthy, postmenopausal women.

The observational study is looking for predictors and biological markers for disease and is being conducted at more than 40 cen-

ters across the United States, while the community prevention study, which has ended, sought to find ways to get women to adopt healthful behaviors and was done with the Federal Government's Centers for Disease Control and Prevention.

WHI's three clinical trials, conducted at the same U.S. centers, are designed to test the effects of postmenopausal hormone therapy, diet modification, and calcium and vitamin D supplements on heart disease, osteoporotic fractures, and colorectal cancer risk.

The postmenopausal hormone therapy clinical trial has two parts. The first involved 16,608 postmenopausal women with a uterus who took either estrogen plus progestin therapy or a placebo. The second involves 10,739 women who have had a hysterectomy and are taking estrogen alone or a placebo.

The estrogen plus progestin trial used 0.625 milligrams of conjugated equine estrogens taken daily plus 2.5 milligrams of medroxyprogesterone acetate taken daily (Prempro). Two key reasons that that combination was chosen are: It is the mostly commonly prescribed form of the combined hormone therapy in the United States, and, in several observational studies, it had appeared to benefit women's health.

The women in the WHI estrogen plus progestin study were aged 50 to 79. They enrolled in the study between 1993 and 1998. Their health was carefully monitored by an independent panel, called the Data and Safety Monitoring Board (DSMB).

The study's main goal was to see if the therapy would help prevent heart disease and hip fractures. Another goal was to see if those possible benefits were greater than the possible risks from breast cancer, endometrial (or uterine) cancer, and blood clots.

The study was to have continued until 2005. However, it was stopped in July 2002 because the DSMB found an increased risk of breast cancer and that, overall, risks from use of the hormones

outweighed and outnumbered the benefits. "Outnumbered" means that more women had adverse effects from the therapy than benefitted from it. The key results are shown in Boxes 9 and 10.

These results show both risks and benefits from use of the estrogen

plus progestin therapy. The key adverse effects were more cases of breast cancer, heart attacks, strokes, and blood clots. The main benefits were fewer hip and other fractures and cases of colorectal cancer.

Additionally, there was no increase in deaths from breast

Box 14

Postmenopausal Hormone Therapy and Ovarian Cancer Risk

Early studies of postmenopausal hormone therapy found inconsistent results about its effect on the risk of ovarian cancer: Some reported increased risk with estrogen use, while others reported no effect or even a protective one. Most of those studies were relatively small and did not take into account the key risk factors for ovarian cancer (see Box 15).

More recently, two large observational studies have indicated that long-term estrogen use increases the risk of ovarian cancer. It's important to keep in mind that observational studies do not prove that a treatment causes a disease (see Box 6). The evidence from these studies is cautionary, not definitive.

Here's more on the studies:

- One study followed 211,581 postmenopausal women from 1982-1996. Of those, 44,260 had used estrogen-only hormone therapy; the rest did not use hormone therapy. None of the women had had a hysterectomy, ovarian surgery, or cancer. Those with 10 or more years of estrogen use had an increased risk of dying from ovarian cancer—and, while the risk decreased somewhat long after use was stopped, it was still higher than that of women who had never used estrogen-only therapy.
- Another study followed 44,241 women from 1979-1998. It found that estrogen-only therapy increased the risk of ovarian cancer. Women who used estrogen alone for 10 or more years had an 80 percent higher risk of ovarian cancer than women who had never used the hormone therapy; women who used estrogen alone for 20 or more years had a 220 percent higher risk than women who had never used hormone therapy.

The study found no increased risk of ovarian cancer for users of estrogen plus progestin. However, few women in the study had used the combination therapy for more than 4 years.

More research is needed to see if estrogen plus progestin affects ovarian cancer risk—and on other aspects of postmenopausal hormone use. For instance, another recent study found that estrogen alone or estrogen plus progestin used on a sequential basis increased the risk for ovarian cancer, while estrogen plus progestin used continuously did not.

Box 15

Risk Factors for Ovarian Cancer

About 1 in 57 American women will develop ovarian cancer. Most will be over age 50, but younger women also can develop the disease.

Here are some factors that increase or decrease the risk of ovarian cancer:

Increases risk–

- Age–risk increases as a woman ages
- Family history of ovarian cancer–higher risk if mother or sister has had ovarian cancer; somewhat higher risk if other relatives, such as grandmother, aunt, or cousin, have developed ovarian cancer
- Postmenopausal hormone therapy–may increase risk
- Fertility drugs
- Personal history of breast and/or colon cancer

Decreases risk–

- Oral contraceptives–the longer the use, the lower the risk may be and the decrease may last after use has ended
- Childbearing and breast-feeding
- Tubal ligation (sterilization) or hysterectomy
- Prophylactic (to prevent or protect) oophorectomy (surgery to remove one or both ovaries)

cancer or from other causes. Further, there was no increase in the risk of endometrial cancer. Here's more on the findings–to better understand them, see “Putting It All Together” on page 13, as well as Box 11:

- **Breast cancer.** The increased risk of breast cancer appeared after 4 years of hormone use. After 5.2 years, estrogen plus progestin resulted in a 26 percent increase in the risk of breast cancer–or 8 more breast cancers each year for every 10,000 women. Women who had used estrogen plus progestin before entering the study were more likely to develop breast cancer than others, indicating that the therapy may have a cumulative effect.
- **Heart attack.** For heart attack, the risk began to increase in the first year of estrogen plus progestin use and

became more pronounced in the second year. After 5.2 years, there were 29 percent more heart attacks in the estrogen plus progestin group than in the placebo group–or 7 more heart attacks each year for every 10,000 women. Unlike HERS, which involved women with heart disease, the increased risk from estrogen plus progestin did not go back down again.

- **Stroke.** For the first time, estrogen plus progestin was shown to cause more strokes in healthy women. By the end of the study, the estrogen plus progestin group had 41 percent more strokes than the placebo group–or 8 more strokes each year for every 10,000 women.
- **Blood clots.** The risk of total blood clots was greatest during the first 2 years of hormone use–four times higher than

that of placebo users. By the end of the study, it had decreased to two times greater–or 18 more women with blood clots each year for every 10,000 women.

- **Fractures.** Estrogen plus progestin reduced hip fractures by 34 percent–or 5 fewer hip fractures for every 10,000 women. This is the first solid evidence from a clinical trial that hormone therapy, in helping to prevent bone loss and osteoporosis, protects women against fractures.
- **Colorectal cancer.** The therapy also lowered the risk of colorectal cancer by 37 percent–or 6 fewer colorectal cancers each year for every 10,000 women. This reduction appeared after 3 years of hormone use and became more significant thereafter. However, the number of cases of colorectal cancer was

Box 16

What About Birth Control Pills?

The recent findings about the risks of long-term postmenopausal hormone therapy do not apply to use of birth control pills, which have not been found to increase breast cancer risk.

There had been concern about the effect of birth control pills on the risk of breast cancer because, until recently, studies had given conflicting results. For example, a 1996 analysis of 54 small studies had found a slight increase among women who were or had recently used oral contraceptives. But the 54 studies differed in quality and some included oral contraceptive preparations no longer in use. Other studies, such as the 1986 "Cancer and Steroid Hormone" (CASH) study, had found no increased risk.

In June 2002, findings of the "Women's Contraceptive and Reproductive Experiences Study" (also called the Women's CARE Study) were released and showed no increased risk of breast cancer, regardless of length of oral contraceptive use, timing of use, age at use, or the users' risk factors for developing breast cancer. The study, supported by the NIH's National Institute of Child Health and Human Development, involved more than 9,257 women between the ages of 35 and 64. The women were interviewed about their contraceptive use.

Oral contraceptives do pose risks, however: Combination oral contraceptives increase the risk of blood clots. Oral contraceptives should not be used if you are at an elevated risk for blood

clots because of diabetes or another condition, or if you smoke. Taking oral contraceptives and smoking increases your risk for heart attack and stroke.

Oral contraceptive use has benefits too: It can reduce the risk of ovarian cancer, endometrial cancer, colorectal cancer, pelvic inflammatory disease (an infection that can lead to infertility), and osteoporosis.



relatively small, and more research is needed to confirm the finding.

The findings are important for several reasons: As a clinical trial, they establish a causal link between use of the particular hormone therapy and its effects on diseases. Further, the findings finally offer some firm guidance to the millions of American women who have a uterus and may consider taking the drugs—6 million already use a form of combination therapy. And, the results apply broadly—the study found no differences in risk by prior health status, age, or ethnicity.

The findings do not apply to postmenopausal use of estrogen alone. That arm of the study, which used 0.625 mg per day of conjugated equine estrogen (Premarin), did not have the same increased breast cancer risk and continues.

However, an observational study, supported by the NIH's National Cancer Institute (NCI), recently found that estrogen-only therapy appeared to increase the risk of ovarian cancer (see Box 14). But other, similar studies have not found such an increased risk, and the possible relationship between estrogen use and ovarian cancer remains unclear. WHI participants

were informed of these findings, and the results were reviewed for their significance to the study's continuation.

Putting It All Together

How can you sort through the benefits and risks and make a good decision about whether or not to use postmenopausal hormone therapy? Here are several points to help you evaluate the findings:

First, it's important to know that, because the study involved healthy women, only a small number of them had either a negative or positive effect from estrogen plus progestin therapy.

Talking With Your Doctor

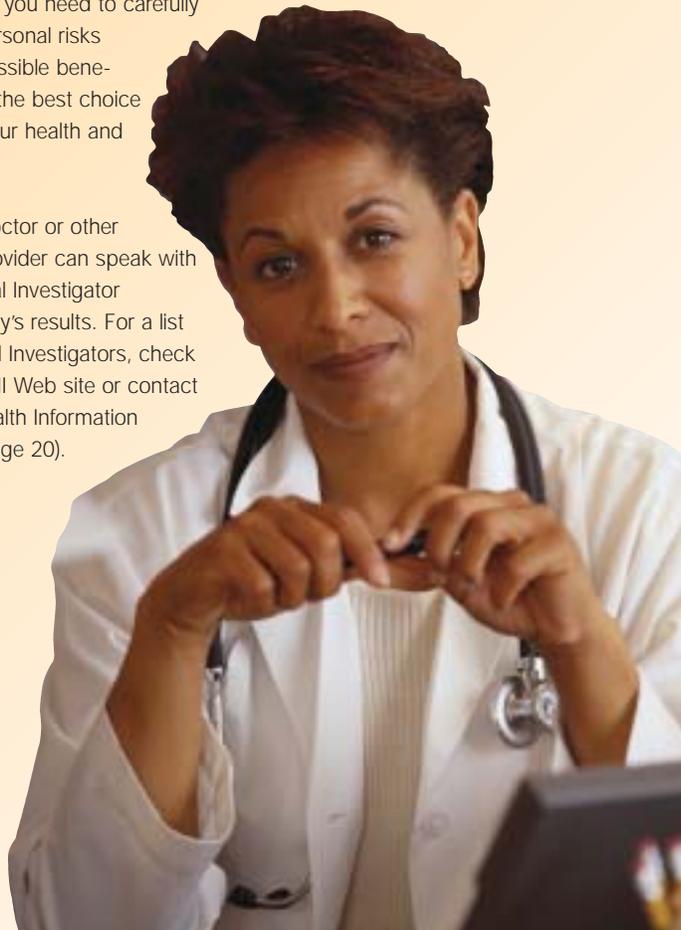
It's important to be involved in your health care. Ask questions and express your concerns. Here are some questions that may help you talk with your health care provider about hormone therapy:

- Why am I taking hormone therapy? Or why should I take hormone therapy?
- Which hormone therapy am I on?
- What are my risks for heart disease, breast cancer, and osteoporosis?
- Should I stop taking the hormone therapy?
- What's the best way for me to stop? What side effects will I have?
- Is there an alternative therapy that I can use long-term?
- What alternatives can help me prevent heart disease?
- What alternatives can help me prevent osteoporosis?
- What can I do to keep menopausal symptoms from returning?

Your risk for heart disease, osteoporosis, and colorectal cancer may change over time. So remember to regularly review your health status with your doctor or other health care provider.

It's also important to bear in mind that your doctor or other health care provider may not be able to answer all of your questions—many questions about postmenopausal hormone use remain. For instance, it's not yet known if increases in disease risk caused by long-term use of estrogen plus progestin drop after use stops. As with any treatment, you need to carefully weigh your personal risks against the possible benefits and make the best choice possible for your health and lifestyle needs.

Finally, your doctor or other health care provider can speak with a WHI Principal Investigator about the study's results. For a list of the Principal Investigators, check the NHLBI WHI Web site or contact the NHLBI Health Information Center (see page 20).



The percentages describe what would happen to a whole population—not to an individual woman. For example, the increased risk of breast cancer for the women in the WHI study who were taking the estrogen plus progestin therapy was less than a tenth of 1 percent each year.

But if you apply that increased risk to a large group of women and over several years, then the number of women affected becomes an important public health concern. As noted, about 6 million American women take estrogen plus progestin therapy. That would translate into nearly 6,000 more cases of breast cancer every year—and, if all of the women took the therapy for 5 years, that might result in 30,000 more cases of breast cancer.

Second, bear in mind that percentages aren't fate. Whether expressing risks or benefits, they do not mean you will develop a disease. Many factors affect that likelihood, including your lifestyle and other environmental factors, heredity, and your personal medical history.

Finally, realize that most treatments carry risks and benefits. No one can make a treatment choice for you. Talk with your doctor or other health care provider and decide what's best for your health and quality of life. Begin by finding out your personal risk profile for heart disease, stroke, breast cancer, osteoporosis, colorectal cancer, and other conditions (see Boxes 7, 8, 12, 13, 15, 18, and 20). Discuss quality of life issues and alterna-

Box 18

Your Heart Disease Risk Profile

One in three American women dies of heart disease. Heart disease kills more American women than any other cause. It also can lead to disability and decrease one's quality of life. Yet, many women don't take the threat of heart disease seriously.

But menopause is a time when you need to get very serious about heart disease because that's when your risk for it starts to rise. So, it's more important than ever to talk with your health care provider about how to lower your risk of heart disease—or, if you already have it, to keep it under control. Ask about your "heart disease profile," a check of the heart disease risk factors you already have or are at an increased risk of developing.

Risk factors are behaviors or conditions that increase your chance of developing a disease. The more risk factors you have, the greater your chance of developing the disease. For heart disease, the risk factors don't just add their risks—they multiply them. So it's vital to prevent them or, if you already have any, to keep them under control.

Fortunately, most heart disease risk factors can be prevented or controlled. Here's a breakdown of both types:

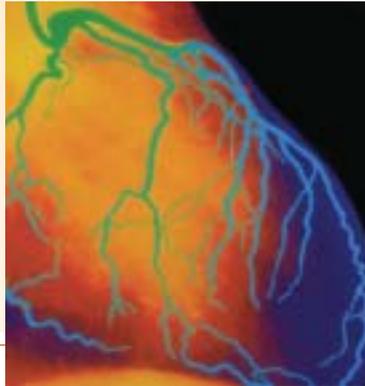
Risk factors beyond your control—

- Being age 55 or older.
- Having a family history of early heart disease—this means having a mother or sister who has been diagnosed with heart disease before age 65, or a father or brother diagnosed before age 55

Risk factors you can control—

- Cigarette smoking
- High blood cholesterol
- High blood pressure
- Diabetes (high blood sugar)
- Overweight/obesity
- Physical inactivity

For more on how to start reducing your heart disease risk, see the resources list on page 20.



hormone therapy. Here it is, along with advice for short-term hormone use to relieve menopausal symptoms:

Short-term estrogen alone or estrogen plus progestin therapy—

- “Short-term” means the shortest time needed to manage menopausal symptoms. The benefits of such use could outweigh any risks for you. Most women use the hormone therapy for 2 to 3 years. However, some may require a longer period of treatment. Talk with your health care provider about your personal risks and needs.

Long-term estrogen plus progestin therapy—

- Do not use estrogen plus progestin therapy to prevent heart disease. The new findings show that it doesn't work. In fact, the therapy increases the chance of a heart attack or stroke. And it increases the risk of breast cancer and blood clots.

What can you do instead?

Talk to your health care provider about other ways to prevent heart disease and stroke that have been proven to be safe and effective. These include lifestyle changes and such drugs as cholesterol-lowering statins and blood pressure medications. Lifestyle changes include: not smoking, maintaining a healthy weight, being physically active, and managing diabetes.

tives to postmenopausal hormone therapy. Box 17 will help you talk with your health care provider. Then weigh every factor carefully and choose the best option for your health and quality of life. And keep the dialogue going—your health status can change and so can your choice.

Advice About Postmenopausal Hormone Therapy

While many questions remain, the new WHI findings provide the basis for some advice about the use of postmenopausal

Box 19**Recommended Daily Intakes of Calcium and Vitamin D**

Age	Vitamin D	Calcium
19-50	200 IU*	1,200 mg**
51-70	400 IU*	1,200 mg**
70+	600 IU*	1,200 mg**

Note: IU=International Units

* not to exceed 2,000 IU

**not to exceed 2,500 mg

Another key part of this is to follow a healthy eating plan that has a variety of foods and is low in saturated fat and cholesterol and moderate in total fat. In addition, limiting how much salt and other forms of sodium you eat will help keep your blood pressure at a healthy level.

- Do not use long-term postmenopausal hormone therapy if you already have heart disease. Such use increases the risk of blood clots. It also increases the risk of heart attack in the first year of therapy.
- To prevent osteoporosis, talk with your health care provider about what your personal risks and benefits would be from estrogen plus progestin therapy. Weigh any benefits against your risk of heart disease, stroke, and breast cancer. Ask about alternate approaches that are considered safe and effective in preventing osteoporosis and fractures. These include oral biphosphonates, such as alendronate

(or Fosamax) and risedronate (or Actonel), and selective estrogen receptor modulators (SERMs), such as raloxifene (or Evista). SERMs are also known as designer estrogens. They are substances that have estrogen-like effects on some tissues and anti-estrogen effects on others.

Other steps to prevent osteoporosis include consuming enough calcium and vitamin D (see Box 19), being physically active, especially with weight-bearing exercises (such as walking, jogging, playing tennis, and dancing), not smoking, and limiting how many alcoholic beverages you drink. Smoking and drinking alcohol increase your risk of osteoporosis. For more on osteoporosis, see Box 20.

Long-term estrogen-only therapy–

- The WHI has not yet issued findings about the health risks and benefits of long-term use of estrogen-only

therapy. Consult your health care provider about your personal health profile and needs.

General advice–

- Whether or not you decide to use postmenopausal hormone therapy, you should keep your regular schedule of mammograms, and breast and clinical exams.
- In addition to having regular mammograms, you should protect your health by having certain other tests done too (see Box 21). These include tests for high blood pressure, high blood cholesterol, high blood glucose (sugar), bone mineral density, and overweight.
- If you stop taking hormone therapy and your menopausal symptoms return, consider alternative treatments (see Boxes 4). Be aware that some of these remedies have not been proved effective or safe.

How Do I Stop Postmenopausal Hormone Therapy?

You should talk with your health care provider about whether or not stopping postmenopausal hormone therapy would be good for you. Also ask about the best way to discontinue the treatment. You can stop abruptly or by gradually reducing the dose over several months.

However, by abruptly stopping the medication, you may have

Box 20

Boning Up On Osteoporosis

More than 8 million American women have osteoporosis—and millions more have lost so much bone that they're likely to develop it.

Osteoporosis can happen at any age but the risk grows as you get older. The first noticeable sign of osteoporosis is often losing height or having a bone break easily. Other signs can be changes in the shape of the spine, prolonged severe pain in the middle of the back, and tooth loss.

Risk factors of osteoporosis include:

- Age—risk increases as you grow older
- Being a woman—women have less bone tissue and lose bone faster than men
- Body size—small, thin-boned women are at greatest risk
- Ethnicity—white and Asian women are at highest risk
- Family history—having parents with a history of fractures
- Sex hormones—abnormal absence of menstrual periods (amenorrhea) or menopause
- Anorexia
- Lifetime diet low in calcium and vitamin D
- Certain medications, such as glucocorticoids (prescribed for various diseases, including arthritis, asthma, and lupus) or some anticonvulsants
- Physical inactivity or extended bed rest
- Cigarette smoking
- Excessive use of alcoholic beverages

If you think you're at risk for osteoporosis or if you're menopausal or older, you may want to ask your doctor or other health care provider about having a test called a DXA-scan (dual-energy x-ray absorptiometry). It measures spine, hip, or total body bone mineral density, or how solid bones are. The results can show the presence and severity of osteoporosis, or if you're at risk of developing it or having fractures.

You can prevent osteoporosis. The key steps are to follow an eating plan that's rich in calcium and vitamin D and be sure to get regular weight-bearing exercises. Calcium and vitamin D intake can be taken as supplements but check with your health care provider first. Too much of either can cause problems. Recommended daily intakes of calcium and vitamin D are given in Box 19. Good food sources of calcium include lowfat dairy foods, canned fish with bones, such as salmon and sardines, dark-green leafy vegetables, such as broccoli, kale, and collards, calcium-fortified orange juice, and breads made with calcium-fortified flour. Vitamin D is made by the body—being in the sun 20 minutes a day

helps most women make enough. But it's also found in eggs, fatty fish (such as sardines, mackerel, and salmon), and cereal and milk fortified with vitamin D. Weight-bearing exercises—done three to four times a week—that help prevent osteoporosis include walking, jogging, stair-climbing, weight training, tennis, and dancing.

It's also important not to smoke and to limit how many alcoholic beverages you drink. Smoking causes the body to make less estrogen, which protects bones. Too much alcohol can put you at risk for falling and breaking bones.

Osteoporosis is treated by stopping bone loss with lifestyle changes and medication. Hormone therapy has been used to prevent and treat osteoporosis. But other drugs are available:

- Raloxifene is a SERM. It may cause hot flashes and blood clots.
- Alendronate (brand name Fosamax) and risedronate (brand name Actonel) are bisphosphonates, drugs that slow the breakdown of bone and may increase bone density. Side effects may include nausea, heartburn, and pain in the stomach.
- Calcitonin is a naturally occurring non-sex hormone that increases bone mass in the spine. It is used for women who are at least 5 years beyond menopause and is taken by injection or nasal spray. The injection may cause an allergic reaction and has some unpleasant side effects, including flushing of the face and hands, urinating often, nausea, and skin rash. The nasal spray may cause a runny nose.



Check It Out

Here's a prescription for better health:

- Blood pressure—healthy women should have it checked every 2 years; others may need it checked more often.
- Lipoprotein profile—checks blood levels of LDL, HDL, total cholesterol, and triglycerides; healthy women should have it once every 5 years.
- Blood glucose—tests blood levels of glucose (a sugar) and indicates risk for diabetes; healthy women age 45 and older should have it, especially if they are overweight; if it's normal and women are healthy and not overweight, it should be taken again in 3 years, while others will need it more often.
- Overweight and obesity check—this is done by calculating your body mass index (BMI) and measuring your waist circumference. BMI is a measure of your weight relative to your height, while waist circumference measures abdominal fat. Box 22 tells you how to calculate BMI. A BMI of 25 or higher is overweight or obese. For women, a waist circumference of more than 35 inches indicates an increased risk for heart disease and other conditions. Your health care provider also will check you for other risk factors and conditions associated with obesity to determine the best treatment.
- Mammogram—a special x ray of the breast; healthy women age 40 and older should be screened for breast cancer with mammography once every 1 to 2 years; studies show screening is especially important for those aged 50-69; women also should do breast self-exams and have their doctor or health care provider do a clinical breast exam during routine physical exams.
- Pap Smear—this test checks a sample of cervical cells for changes that may lead to cancer; begin by having it as part of an annual gynecological exam and, if normal 3 years in a row, talk with your doctor about how often to have it after that.
- Colonoscopy—examines the inside of the colon and rectum using a thin, lighted tube called a colonoscope; healthy women should have it once every 5 years starting at age 50.
- Bone density—this x ray measures bone thickness and strength; postmenopausal women with one or more risk factors for osteoporosis (besides menopause) or who suffer fractures, and women age 65 and older regardless of added risk factors should have this test.
- Electrocardiogram (EKG or ECG)—this tests the heart's electrical activity as it beats; women over age 40 should have a baseline EKG.



menopause-like symptoms. Gradually weaning your body off the medication can ease this.

Questions Remain

The new findings have provided some details about the dangers and benefits of postmenopausal hormone therapy, but many

questions remain. The WHI is following women in the estrogen plus progestin trial to see if and when increased risks and benefits decline after use of the therapy ends. Also, in 2005, the WHI

is expected to release key information about the effects of postmenopausal estrogen-only therapy.

Other WHI studies include:

- The observational study is examining other forms of hormone therapy, including other estrogens, progestins, and SERMs.
- The postmenopausal hormone therapy trial has been investigating hormones' effects on memory. While the estrogen plus progestin part of that study ended, the estrogen-only arm continues.
- A WHI substudy is examining hormones' ability to prevent or delay Alzheimer's disease and other forms of dementia.

Additionally, scientists funded by the NHLBI, the National Cancer Institute, the National Institute on Aging, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Center for Complementary and Alternative Medicine, the National Institute of Mental Health, and other units of the NIH are supporting research on the effects of postmenopausal hormones and alternative therapies on the symptoms of menopause and conditions that occur after menopause. The research includes studies of: the effects of soy phytoestrogens on cardiovascular disease and osteoporosis, postmenopausal use of phytoestrogens on cardiovascular risk and health, black cohosh and

Box 22

Check Your BMI

Body mass index—or BMI—relates weight to height and is used as an indicator of total body fat. It is used with waist circumference to see if you're overweight or obese.

To find your BMI, use the method below or go to the Aim For A Healthy Weight Web page at www.nhlbi.nih.gov/health/public/heart/obesity/lose_wt/index.htm, which offers tables and an automatic calculator.

Here are three steps to find your BMI:

- Step 1 Multiply your weight* in pounds by 703.
- Step 2 Divide the answer by your height in inches.
- Step 3 Divide the answer again by your height in inches.

The BMI score means:

18.5-24.9	Normal
25.0-29.9	Overweight
30.0 and above	Obese

**Weight wearing underwear but no shoes*



antidepressants on hot flashes, botanical dietary supplements on women's health, plant estrogens on breast cancer, and estrogen on cognition.

For More Information

The following resources can help you learn more about hormone therapy-related topics:

National Heart, Lung, and Blood Institute

National Institutes of Health NHLBI Health Information Center

P.O. Box 30105
Bethesda, MD 20824-30105
Phone: (301) 592-8573
TTY: (204) 629-3255
Fax: (301) 592-8563
Web site: www.nhlbi.nih.gov
WHI Web site: www.whi.org

National Cancer Institute National Institutes of Health

Phone: (800) 4-CANCER
(800-422-6237)
Web site: www.nci.nih.gov

National Center for Alternative and Complementary Medicine

National Institutes of Health

NCCAM Clearinghouse
P.O. Box 7923
Gaithersburg, MD 20898-7923
Phone: (888) 644-6226
TTY: (866) 464-3615
International Phone: (301) 519-3153
Fax: (866) 464-3616
Web site: www.nccam.nih.gov

National Institute on Aging National Institutes of Health

Phone: (800) 222-2225
TTY: (800) 222-4225
Web site: www.nia.nih.gov

National Institute of Arthritis and Musculoskeletal and Skin Diseases

National Institutes of Health NIAMS Information Clearinghouse

1 AMS Circle
Bethesda, MD 20892-3675
Phone: (301) 495-4484 or
(877) 226-4267
TTY: (301) 565-2966
Fax: (301) 718-6366
Web site: www.niams.nih.gov

NIH Osteoporosis and Related Bone Diseases~National Resource Center

1232 22nd Street, NW
Washington, DC 20037-1292
Phone: (202) 223-0344 or
(800) 624-BONE
Fax: (202) 293-2356
TTY: (202) 466-4315
Web site: www.osteo.org

National Institute of Child Health and Human Development

National Institutes of Health NICHD Clearinghouse

P.O. Box 3006
Rockville, MD 20847
Phone: (800) 370-2943
Fax: (301) 984-1473
Email: NICHDclearinghouse@mail.nih.gov
Web site: www.nichd.nih.gov

Food and Drug Administration Department of Health and Human Services

5600 Fishers Lane
Rockville, MD 20857
Phone: (888) INFO-FDA
(888-463-6332)
Web site: www.fda.gov

Office on Women's Health Department of Health and Human Services

200 Independence Avenue, SW
Room 730B
Washington, DC 20201
Phone: (202) 690-7650
Fax: (202) 205-2631
Web site: www.4women.gov/owh

National Women's Health Information Center Department of Health and Human Services

8550 Arlington Boulevard
Suite 300
Fairfax, VA 22031
Phone: (800) 994-WOMAN
(800-994-9662)
or (888) 220-5446
Web site: www.4women.gov

North American Menopause Society

P.O. Box 94527
Cleveland, OH 44101
Phone: (440) 442-7550
Automated Consumer Request
Line: (800) 774-5342
Fax: (440) 442-2660
E-Mail: info@menopause.org
Web site: www.menopause.org

Alliance for Aging Research

2021 K Street, NW
Suite 305
Washington, DC 20006
Phone: (202) 293-2856
Fax: (202) 785-8574

American Heart Association National Center

7272 Greenville Avenue
Dallas, TX 75231
Phone: (800) AHA-USA-1
(800-242-8721)
Web site: www.americanheart.org

American Stroke Association National Center

7272 Greenville Avenue
Dallas, TX 75231
Phone: (888) 4-STROKE
(888-478-7653)
Web site: www.strokeassociation.org

National Osteoporosis Foundation

1232 22nd Street, NW
Washington, DC 20037-1292
Phone: (202) 223-2226
Web site: www.nof.org



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service
National Institutes of Health
National Heart, Lung, and Blood Institute

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